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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,040	12/30/2005	Brian G. Van Ness	09531-109US1	9035

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
08/31/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/532,040	VAN NESS ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-32* is/are pending in the application.

4a) Of the above claim(s) *9-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 6/4/10 has been entered. New claims 30-32 have been added. Claims 1, and 3-32, claim 2 having been previously canceled, are now pending in the instant application.

The previous office actions acknowledged that applicant had elected without traverse the invention of Group I, and the species Bcl-xl in the responses received on 2/26/08 and 5/28/08. Claims 9-29 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 1, 3-8, and 30-32 are therefore currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Claim Rejections - 35 USC § 103

The rejection of previously pending and new claims 1, 3-7, and 30-32 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, is maintained. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their arguments that the rationale for combining the teachings of the cited references does not apply as substitution of the kappa enhancer for the heavy chain enhancer is not a simple substitution of one known element for another with predictable results. According to applicant, Adams teaches away from using the kappa enhancer by teaching that the heavy chain enhancer resulted in higher tumor incidence that the kappa enhancer. The applicant further argues that oncogene transformation of plasma cells required the combination of an Ig promoter with the kappa enhancer.

In response, regarding the development of different types of B cell malignancies, the applicant is reminded that the transgenic mouse as claimed does not contain any limitation regarding tumor development. In addition, none of claims 1, 3-7, or 30-32 requires a kappa promoter. As for the argument that Adams teaches away from using the kappa enhancer by teaching that the heavy chain enhancer resulted in higher tumor incidence that the kappa enhancer, the previous office actions responded that Grillot et al. only differs from the claimed invention by using an Ig heavy chain enhancer instead of an Ig kappa 3' enhancer. Adams et al. was cited to supplement the teachings of Grillot et al. by teaching that both the Ig heavy chain enhancer and the Ig kappa chain enhancer are effective in driving B cell specific heterologous transgene expression in transgenic mice (Adams et al., pages 533-534 and 537). As such, since the Ig kappa chain enhancer, like the Ig heavy chain enhancer, is capable of directing B cell specific expression of heterologous transgenes in transgenic mice, it is maintained that it would have been *prima facie* obvious to the skilled artisan at the time of filing to substitute the Ig kappa enhancer taught by Adams et al. for the Ig heavy chain enhancer in the constructs for making a transgenic mouse according to Grillot et al. with a reasonable expectation of success in using

such a construct to produce a transgenic mouse exhibiting a phenotype of expanded mature B cells and plasma cell populations, as such a replacement represents nothing more than simple substitution of one known element for another to obtain predictable results. The functional similarity referred to in previous office actions was the clear demonstration by Adams that both the heavy chain and kappa chain enhancer effectively drive B cell specific heterologous transgene expressing in transgenic mice. Further, as stated in the previous office actions, the motivation to combine the teachings of the cited references need not be supported by a finding that the prior art suggested that the combination claimed by the applicant was the preferred, or most desirable combination over the other alternatives. *In re Fulton*, 391 F.3d 1195, 73 USPQ2d 1141 (Fed. Cir. 2004).

Turning to the amendments to the claims, independent claim 1 has now been amended to add new phenotypic limitations to the transgenic mouse including: that the transgenic mouse exhibit elevated serum levels of IgM, IgG1, IgG2b, IgA, and IgE isotypes as compared with a corresponding wild-type mouse; that the transgenic mouse is capable of surviving at least 60 days; and, that a serum sample from said transgenic mouse does not exhibit a clonal spike of gamma immunoglobulin. New dependent claims 30-32 further add that the mice exhibits kidney pathology, or lymphocytic pathology, or that the T cell independent antigen-specific immunoglobulin after antigenic challenge is greater in the transgenic mouse than a wild-type mouse. The applicant argues that neither Grillot et al. nor Adams et al. teaches or provides a reasonable expectation for these characteristics.

In response, it is first noted that Grillot et al. does in fact teach that transgenic mice expressing B cell specific Bcl-xL under control of the heavy chain enhancer were alive at 5

months, which is far longer than 60 days such that the skilled artisan would have had a reasonable expectation that a transgenic mouse expressing B cell specific Bcl-xL under control of the kappa light chain enhancer would also live for longer than 60 days. In regards to the rest of the added phenotypic limitations, it is acknowledged that Grillot et al. does not report testing the serum of the transgenic mice for the levels of particular Ig subtypes, does not report on the pathologies of the kidney or lymphocyte populations in these mice, and does not teach the effects of immunizing the mice with T cell independent antigens. However, the absence of such teachings by itself does not provide evidence of nonobviousness or the unpredictability of any one of these phenotypes, nor does it demonstrate that Grillot et al. nor Adams et al. teaches away from transgenic mice exhibiting any of these phenotypes. A showing of unexpected results must be based on evidence, not argument or speculation. *In re Mayne*, 104 F.3d 1339, 1343-44, 41 USPQ2d 1451, 1455-56 (Fed. Cir. 1997) (conclusory statements that claimed compound possesses unusually low immune response or unexpected biological activity that is unsupported by comparative data held insufficient to overcome *prima facie* case of obviousness).

In fact, as Grillot et al. does teach that transgenic mice expressing B cell specific Bcl-xL under control of the heavy chain enhancer exhibit increased numbers of all B cell subtypes tested, this result would provide the skilled artisan with a reasonable expectation that the increase in plasma B cell numbers would lead to an increase in all immunoglobulin subtypes secreted by these cells. As for the absence of a clonal spike of gamma immunoglobulin, there is no suggestion in the prior art or any evidence of record to suggest that Bcl-xL overexpression in B cells would lead to such a spike. Thus, the skilled artisan at the time of filing would have

reasonably expected transgenic mice expressing B cell specific Bcl-xL under control of the kappa light chain enhancer to lack such a clonal gamma immunoglobulin spike.

Ultimately, the applicant is reminded that the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). The applicant is also reminded that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

Therefore, for the reasons set forth above, applicant's arguments are not found persuasive and the rejection of record stands.

The rejection of claim 8 under 35 U.S.C. 103(a) as being unpatentable over Grillot et al. (1996) J. Exp. Med., Vol. 183, 381-391, in view of Adams et al. (1985) Nature, Vol. 318, 533-538, applied to claims 1, 3-7, and 30-32 above, and further in view of Miller et al. (1992) Immunogenetics, Vol. 35, 24-32 is maintained. Applicant's amendments and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their arguments regarding the teachings of Grillot et al. and Adams et al. and further states that Miller et al. does not overcome the deficiencies of Grillot et al. and Adams et al. In response, the arguments regarding the teachings of Grillot et al. and Adams et al. have been discussed in detail above and have not been found persuasive in overcoming the rejection of record. Therefore, the rejection of record stands.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that

all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633